UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,023	07/11/2001	Jack R. Wands	21486-032DIV1	3871

7590 02/07/2002

MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, MA 02111

EXAMINER
YU, MISOOK

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/903,023	Applicant(s) WANDS ET AL.	
	Examiner Misook Yu	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2001 and 12 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,28 and 39-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,28 and 39-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-9, 28, and 39-54 are pending and Claims 1-9, 28, and 39-54 are examined on merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-8, 39, 40, 43, 45, 46, 51, and 52 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are determination steps to achieve the purpose stated in the preamble; it needs relating steps linking the detection of antigen-antibody complex to diagnosing a malignant neoplasm. See the construction of claim 9 of the instant application. drop

Claim 41, 42, 44, 47-50, 53, and 54 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are determination steps to achieve the purpose stated in the preamble; it needs relating steps linking the detection of antigen-antibody complex to diagnosing a malignant neoplasm. See the construction of claim 9 of the instant application. For the purpose of this office action, the examiner will assume that any detection of the antigen-antibody complex leads to diagnosis of a malignant tumor. However, this treatment does not relieve applicants of the burden of response to this rejection. drop

In addition, claims 1, 9, and 41 recite "under conditions sufficient to form an antigen-antibody complex" but it is not clear what the metes and bounds are for under conditions sufficient to form an antigen-antibody complex. drop

Claim 9 recites "a normal control level" but it is not clear what the metes and bounds are for "a normal control level" of HAAH in a bodily fluid of a mammal. drop

Claim 28 recites "killing tumor cell" but it is not clear what the metes and bounds are for killing tumor cell. Is the cytotoxic agent linked to an HAAH-specific antibody used to kill tumor cell inside live human, inside live mice, tumor cell from tumor cell lines, or tumor cell isolated from various mammals? Does the "killing tumor cell" have a therapeutic connotation? Based on the description for the use of the product at page 9 of the specification, the examiner will assume "killing a tumor cell" imply treatment of tumor for the purpose of this examination. However, this treatment does not relieve applicants of the burden of response to this rejection.

cancelled

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, and 39, 40, 43, 45, 46, 51, and 52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1-9, and 39-54 are drawn to method for diagnosis and prognosis of a malignant neoplasm, comprising contacting ***a bodily fluid*** with antibody that reacts with HAAH. However, the specification fails to teach any correlation between presence of HAAH polypeptide present in blood or in other bodily fluid of a mammal and presence of a malignant tumor in a mammal, although previous studies (see C19, C35, C38 of the IDS, all of these references more than one year before the effective filing date of the instant application) as well as the instant specification have established using previously known monoclonal antibody FB50 that high-level HAAH expression in numerous malignant ***tissue samples*** exists. However, the high-level HAAH expression were detected in the specimen obtained from surgical resection of tumor (pages 36, lines 6-23), not from the source recited in the limitation of the instant claims. The specification fails to establish correlation between detection of HAAH polypeptide-antibody complex in bodily fluid to

diagnosis of a malignant tumor. Compare contents of the instant specification and claims to the abstract of Teillac et al. The most urgent issues that the specification has not taught in order to use the instant invention for the purpose stated in the preamble are; (1) does a bodily fluid of a mammal that has a malignant neoplasm contain HAAH polypeptide? If it exists, (2) does the polypeptide in the ***bodily fluid*** and ***tissue samples*** exists as a same form or in a different splicing variant or other modified form to overcome the solubility problem in a bodily fluid? If two different forms exist, then (3) is it possible to use the monoclonal antibody in claims 6-8 to detect the form in a bodily fluid. Detection in table 3 was done by staining tissue samples and looking at the sample under the microscopy. No evidence exists that the HAAH could be detected using the method described in page 14, claims 1-9, and 39, 40, 43, 45, 46, 51, and 52. Because of the limited guidance (no correlation between HAAH tissue overexpression to detection of HAAH in bodily fluid), lack of working examples, and unpredictability of success for diagnosis or prognosis of other cancers using bodily fluid concentration (see the entire abstract of Weg-Remers et al), it is concluded that undue experimentation would be required to use the invention as claimed.

Claims 41, 42, 44, 47, 49, 50, 53, and 54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims 41, 42, 44, 47, 49, 50, 53, and 54 say detecting a HAAH polypeptide antigen-antibody complex in a bodily tissue is sufficient to diagnosis of a malignant tumor but Lavaissiere et al (Table 1) says that the antigen is also present in some normal tissues, especially liver. Therefore, detection of the antigen is not sufficient to diagnosis of cancer. Because of the limited guidance about which type of tissues normally expresses the antigen, lack of working examples for cancer diagnosis using detection of a HAAH polypeptide antigen-antibody complex, and unpredictability of success using the method in claim 41 for diagnosis of hepatocellular carcinoma (claim 47), glioblastoma (claim 53), and neuroblastoma (claim 54), it is concluded that undue experimentation would be required to use the invention as claimed.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for how to make the cytotoxic agent-linked to an HAAH-specific antibody by combining teaching of prior art (see C19 for the HAAH-specific antibody and linking step for U.S. Pat. 5,854,205, column 14, lines 5-15), does not reasonably provide enablement for how to use it to kill tumor cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Although the specification mentions extracellular HAAH at page 8, lines27, there is no evidence in the specification that extracellular HAAH exists. The specification fail to show the cytotoxic agent-linked to an HAAH-specific antibody kills tumor cells of any kind. The specification failed to show any evidence that HAAH is expressed on cell surface although applicant suggests the possibility of epitope exposed on the surface of the cell at page 8, last line of the specification. What is the role of the antibody in the cytotoxic agent-linked to an HAAH-specific antibody if the alleged extracellular HAAH does not exist? Not only tumor cells but normal liver (see material and method section of C32 of the IDS) cells seem to express HAAH. How does the cytotoxic agent-linked to an HAAH-specific antibody preferentially kills tumor cells compared to non-tumor cell (page 9, line 2) while normal cells also express the same enzyme? The specification failed to show any evidence that malignant tumors express the HAAH on the surface while normal cell does not express it on its surface. Because of the limited guidance, lack of working examples, and unpredictability of success for using the cytotoxic agent-linked to an HAAH-specific antibody for killing tumor cells, it is concluded that undue experimentation would be required to use the invention as claimed.

Cancelled

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 41, 42, 44, and 48, 49, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Lavaissiere et al (C19 of the IDS). Lavaissiere et al teaches the active step of claims 41, 42, 44, and 48 in the entire article especially Table 1 using inherently similar antibodies in claim 49 and 50. Lavaissiere et al teaches the detection method of the antigen-antibody complex with immunohistochemical stainig (claim 44) of a bodily tissue of a mammal from a biopsy of a solid tumor (claim 42), cholangiocarcinoma (claim 48) with inherently similar antibodies (claim 49 and 50) to FB-50 mAb which binds to a HAAH polypeptide to form an antigen-antibody complex. Lavaissiere et al further teaches detection of the antigen-antibody complex occurs in the cholangiocarcinoma, but not in the normal bile ducts.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Misook Yu whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu

February 5, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600